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13. ABSTRACT (Maximum 200 words) The Final Proceedings/Report for UNESCO Seminar on Cellular Mechanisms of Beneficial and harmful Effects of Electromagnetic Fields, held 24 September 2000 - 3 October 2000, in Yerevan, Armenia. This is an interdisciplinary conference. Topics included cellular aspects of EMF biological effects and developing adequate methods for estimating the EMF-induced biological effects. The final report is a brief summary of the papers presented there.				
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**UNESCO SEMINAR ON
CELLULAR MECHANISM OF BENEFICIAL AND HARMFUL EFFECTS OF
ELECTROMAGNETIC FIELDS**

September 24 - October 3, 2000, Yerevan, Armenia

R E P O R T

The President of Armenian NAS **Fadey Sargsian** and the Rector of Yerevan State University (YSU) **Radic Martirosian** welcomed participants of the seminar on behalf of the Presidium of Armenian NAS and YSU and gave emphasis to the main object of the meeting, that is to identify the gaps in scientific knowledge and to propose research needs in the area of magnetobiology.

The Deputy of RA Education and Science Minister **Mr. Avetisian** on behalf of the Armenian government, the Deputy of RA Health Minister **Mr. Davtians** on behalf of Armenian public health services and the Secretary-General of National Commission for UNESCO **Mrs. Asaturian** on behalf of the RA Ministry of Foreign Affairs welcomed all the participants.

Dr. Michael Repacholi from WHO Office of Global and Integrated Environmental Health in Geneva added his welcome on behalf of WHO and gave a brief report on the present achievements in the study of EMF biological effects. He also talked about its future plans in this field and the intention to harmonize the EMF standards worldwide. Dr. Repacholi invited Armenian government to.

- Join and participate in WHO's International EMF Project,
- Contribute to the development of common approaches for protecting people from EMF,
- Assist in WHO's efforts to work out harmonized EMF standards.

Dr. Michael Murphy, Chief of the USA Air Force Radiofrequency Radiation Branch, welcomed the delegates of the meeting as the coorganizer of the seminar and expressed his hope that during this multidisciplinary seminar scientists would be able to discuss molecular and cellular mechanisms of EMF biological effect and to work out adequate methods for its estimation.

Dr. Sinerik Ayrapetyan, President of UNESCO Chair - Life Sciences International Educational Center (LSIEC), finalized the opening session by presenting LSIEC short history and objectives. He introduced LSIEC as international research, educational and applied center, the main objectives of which are to promote co-operative research, advanced training and exchange of information in Armenia and other countries of the region; to facilitate collaboration between high-level, internationally recognized researchers and the local scientific community. LSIEC started its activity by organization of short-term international seminars on different fields of life sciences. The first of them related to Pain Study and Management and was organized in 1996; the subject of next one was "Modern Problems of Molecular and Cellular Neuroscience" (1997). Then a seminar on "Modern Problems of Cellular and Molecular Biophysics" was organized in 1998. Thus, the current seminar was the fourth one. During these seminars the students had opportunity to attend the lectures of distinguished scientists from different countries and to communicate with them. The latter was especially helpful for them in choosing their future research fields. Dr. Ayrapetyan expressed his thanks to the co-organizers of the seminar **Dr. Leeka Kheifets**, **Dr. Michael Repacholi**, **Dr. Michael Murphy** and to **Dr. Andrei Pachomov** for their personal efforts in organization of the seminar and for their participation as lecturers. He hoped that the seminar would be as productive as the previous ones.

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The scientific presentations began with **Dr. Ayrapetyan's** lecture on "Cellular Water as a Target for EMF". He presented experimental data according to which cell's water medium serves as the second messenger between EMF and cell metabolism, while the cyclic nucleotides-dependent Na:Ca exchanger is the gate for the metabolic cascade, through which the biological effect of EMF is realized. It was shown, that the distilled water exposure in low frequency (less than 100Hz) EMF and its treatment by vibration leads to the frequency-dependent decrease of its specific electrical conductivity. Moreover, more pronounced effects were observed in the range of 4-10 Hz frequency in both cases. These frequencies were more effective also in the study of DNA water solution optical density (at 260 nm). The treatment of DNA water solutions for 30 min by MV at frequencies of 4 and 10 Hz leads to the optical density decrease to $4,2 \pm 1,1$ % and $4,8 \pm 1,2$ % correspondingly. Prof. Ayrapetyan explained the synergism effect of EMF and MV on water structure because of dipole moment of water molecules. The same frequency "windows" of effectiveness were observed in the study of the effect of nutrient medium previously exposed in EMF or treated by mechanical vibration on bacteria vital functions. However the direction of EMF and MV effects was different, that is to say EMF leads to the increase, while MV has depressing effect on the cell growth. The different effects of these two factors are considered as the evidence that EMF-induced effect can be explained not only by mechanical changing of water structure as it is in case of MV. On the basis of more detailed investigations of EMF biological effect on neuromembrane properties by means of modern neurochemical and biophysical methods (isotope measurement of ionic fluxes, immunoassay method of intracellular cyclic nucleotides estimation, Voltage-Clamp and Patch-Clamp methods for studying the properties of ionic channels) Prof. Ayrapetyan concluded that cGMP-dependent Na:Ca exchanger is an extra sensitive sensor in membrane through which the biological effect of EMF-induced water structure changes is realized.

The subject of "Cellular Water Medium as a Target for EMF" was also the topic of two lectures and five posters presented by Ayrapetyan's coworkers.

Dr. Armine Danielian (LSIEC, Armenia) presented data on static magnetic field (SMF)-induced cell dehydration in norm and pathology and described the possible role of cell hydration in Oncology. Radioactive labeled ouabain was used for estimating the SMF-induced cell volume changes. According to presented data SMF exposure leads to the decrease of ouabain binding both in normal and in cancer glandular tissues of breast cancer patients. However this effect was more pronounced in pathology rather than in norm.

Dr. Grigory Grigorian (LSIEC, Armenia) presented experimental data on the effect of water previously exposed to SMF 0,2T on the behavioral activity of rats, which allowed him to conclude that in spite of the fact that the memory of rats was not effected by magnetized water, their emotional activity was sensitive to it. He considered these data as an additional evidence for the idea that water medium of organism serves as a mediator for magnetic fields effects on animal behavior.

Dr. Leeka Kheifets (EPRI, USA), the coordinator of EMF Research Program at Electrical Power Research Institute, presented a review on EMF health effects. She outlined the impressive epidemiological data on the correlation between the exposure in EMF and the frequency of different diseases emergence, such as childhood leukemia, brain cancer, breast cancer, neurodegenerative and hearth diseases.

Dr. Michael Repacholi (WHO, Switzerland), the coordinator of Occupational and Environmental Health in WHO, presented a lecture on "The Physical Characteristics, Biological Effects and Health Hazard Assessment in Non- Ionizing Radiation". He introduced the International EMF Project in general and the research review of low-level exposure to EMF and their possible health hazards. In the framework of the project studies memory loss, cancer, blood pressure changes, subjective effects, blood brain barrier were among not-established EMF effects. The special subject of the study was the definitions of radiofrequency (RF) biological and health effects. The realized studies had shown that RF had not genotoxic or mutagenic effects and unlikely to initiate cancerogenesis.

Dr. John Dobson (Keele University, UK) had a lecture on "Interactions of Applied Electromagnetic Fields with Biogenic and Biocompatible Magnetic Nanoparticles" and presented data on the distribution and the function of bioferrites in human tissues. According to the data these particles have regulating role in channel function in magnetotactic bacterias and using external magnetic fields could modulate channel function. The study of the correlation between distribution of bioferrites in brain tissue and epileptic activity of brain allowed him to conclude that weak magnetic field stimulation may be useful in early diagnosis of epilepsy and its possible treatment. Dr. Dobson presented experimental data confirming his working hypothesis stating that synthetic magnetic nanoparticles could be used for drugs and gene delivery.

Dr. Michael Murphy (EOARD, USA), Branch Chief of AFRL/HEDR, presented a lecture on "Health and Safety of Exposure to High Peak Power Microwave (HPM) and Ultrawide Band Radiation (UWB)". His talk related to the United States Department of Defense (DoD) support to EMF International and Pan American Health and Safety programs: bioeffects, dosimetry and standards. As DoD is one of the world's largest developers and users of HPM and UWB emitting systems it has the need and obligation to evaluate the potential health and safety impact of human exposure to the emission of the RF radiation systems. DoD chartered group called "Tri-Service Electromagnetic Radiation Panel" (TERP) consists of three members each from the Army, the Navy and the Air Force. TERP focuses on contemporary and future military issues and exposure situations. At present the research group focuses on the possible hazards of pulses with rapid rise-time and wide frequency-content, so called UWB radiation. Dr. Murphy emphasized the modern problems in EMF biological research, dosimetry advances and standard-setting activities. He noted that in RF radiation dosimetry main problem is to create an adequate method for estimation of RF power actually absorbed by biological objects within the exposure. He explained that the US Air Force RF radiation bioeffects program at Brooks AFB operates not only for its own research efforts, but also to facilitate high standard of dosimetry and the study in the field in general.

Dr. Andrei Pakhomov (EOARD, USA) presented data on "Studying High Peak Power Microwave Effects in Excitable Tissues". In the first part of his lecture he described a modern technique for dosimetry of MW developed by him. This method allows to estimate the specific adsorption in vitro experiments by tissues and to separate the thermal effect from non-thermal one. The summary of his study was that MW effect on both extracellular recording of electrical activity of hippocampus slices and hearth pacemaker activities are realized by thermal effect, while a specific effect on them is not observed.

Dr. Armen Karapetyan (LSIEC, Armenia) presented a lecture on "The Influence of EMF on Water and Water Solutions". Theoretical and experimental investigations have shown that cellular water may serve as a target, which leads to the modulation of several physiological processes in the living cell. Cell water structure is complex: free water and surface water close to the biomolecules are not identical. In free water dipoles are oriented randomly and are constantly changing their positions unlike surface water where they are oriented in an ordinary fashion. Recent studies showed that water might be considered as a liquid crystal with an oxygen ordered structure (below 40°C), which is destroyed above 40°C. Moreover external disturbances, such as steady electrical and magnetic fields make crystalline structure of water to obtain proton ordered structure with quite expressed property of ferroelectricity. This process is amplified at the resonance frequency region of water (0-10 GHz) and the dipoles of water molecules are reoriented and oscillated with the same frequency as the incident EMF. The variety of aminoacids and nucleic acids (NA) sequences, the presence of hydrogen bonds in specific sites, structures characterized by strong electric fields and diamagnetic susceptibility anisotropy (α -helices β , B, A, Z forms of DNA, RNA), molecular conformational changes are key elements in determining the way proteins and NA operate. Dr. Karapetyan suggested that this knowledge might be useful for studying the biological effect of EMF.

Dr. Dmitri Tchitchkan (Academy of Postgraduate Education, Belarus) presented experimental data on the role of the nervous system and nitric oxide in the modulating effect of magnetic fields on nociceptive reflexes in endotoxemic rats. The effect of low-frequency magnetic fields on nervous system depending on the functional state of the nociceptive and thermoregulatory systems was studied. Determinative role of the functional state of the nociceptive and thermoregulatory systems in the realization of physiological effects of low-frequency magnetic fields was shown. He presented experimental data on the involvement of the nervous system and nitric oxide in the realization of magnetic field biological effect.

A group of lecturers presented number of experimental models, which can be used as a target for EMF and also valuable for estimating its biological effect

Dr. Valery Arakelian (LSIEC, Armenia) presented a lecture on "The influence of external noise on membrane surface potential", where he developed a new mathematical model according to which the noise oscillation on the mouth of ionic channels can be an extrasensitive target for EMF.

Dr. Nuno Santos (University of Lisbon, Portugal) suggested a number of modern biochemical and biophysical methods: for intracellular Ca concentration measurement and estimation of membrane fluidity by means of fluorescence probe in different cells, for measurement of NO production, the erythrocytes affinity for oxygen, membrane fluidity by fluorescent probe, membrane fluctuation by laser beams, etc.

Dr. Margaret Tzaphildou (University of Ioannina, Greece) presented a mathematical model for estimation of collagen state. She suggested using this model for detecting biological effects of EMF.

Dr. Mohammad Fahim (Delhi University, India) described cardiovascular receptors as extrasensitive target for different factors (temperature, osmotic pressure, biological substances, etc.) and suggested using these receptors for estimating EMF biological effect.

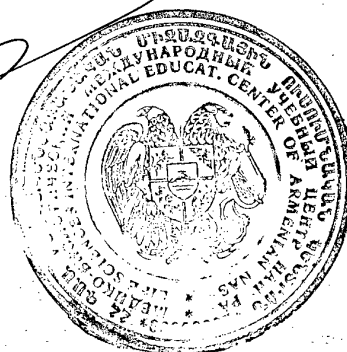
Dr. Natalia Fedirko (University of Lvov, Ukraine) presented data on electrophysiological characteristics of Na:Ca exchange in secretory cells. She suggested the electrogenic Na:Ca exchange as an extrasensitive sensor in cell membrane for EMF.

In the framework of the seminar two "round tables" were organized:

- LSIHES as Educational, Research and Applied Sciences Regional Center,
- EMF Dosimetry, Biological and Health Effects with a View to the Development of Harmonizing EMF Standards Worldwide.

During the first "round table" the research collaboration for realization of the international project on "Cellular and Molecular Mechanisms of EMF Biological Effect" suggested by LSIEC (see appendix 1) was discussed. The second "round table" was organized by Dr. M. Repacholi (WHO) and Dr. V. Davtians (Deputy Minister of Health of RA) and related to the situation of EMF standardization in regional countries presented by LSIEC representatives in India, Iran, Portugal, Greece, Belarus, Ukraine and Georgia. The development of the harmonizing EMF Standards Worldwide was discussed there and in the result of this a Memorandum was signed (see appendix 2) by participants.

Sinerik Ayrapetyan
Org. Committee Chairman



APPENDIX 1

International Project

"Molecular-Cell Mechanisms of Biological Effect of Electromagnetic and Acoustic Waves":

Regional (Western Europe-Asia) EMF Standard Harmonization

Civilization is entering the 21st century, when technical progress brings to the threshold of ecological catastrophe, because the number of unsettled problems is increasing faster than the number of solved ones. In the spectrum of this problem the biological effect of EMF is one of the important from the point of view of human health. Although at present the biological effect of EMF can be considered as a proven fact, the nature of the cellular target for EMF and the cellular mechanisms, through which its effect is realized, is not clear yet. Obtained experimental data on the cellular and molecular mechanisms of EMF in different laboratories are contradictive and difficult for interpretation. Numerous hypotheses on cellular mechanisms have been proposed, but none of them provided a reliable and exhaustive explanation of the experimental funding. It is suggested that the main difficulty to accumulate the experimental data is due to the fact that different laboratories are using different methods to record the EMF-induced biological effect, and later it can be significantly modulated by other factors like as background radiation, acoustic waves, toxins, temperature and other factors. Therefore, it's necessary to work out adequate methods for estimating the EMF-induced biological effect.

During last decades the Biophysics Centre in Yerevan, on the basis of which the Department of Environmental Health of UNESCO Life Sciences International Educational Centre was organized, in collaboration with numerous Armenian life sciences research centres established that Na-K pump and Na:Ca exchanger are power membrane mechanisms, through which the metabolic regulation of membrane excitability, chemoreceptivity and enzyme activity is realized. It was shown that these carrier-driving ionic transporting mechanisms are more sensitive for external physical and chemical signals than channel driving mechanisms. By the study of correlation between EMF-induced water structure changes and the activity of cyclic nucleotides-dependent Na:Ca exchange activity was shown that cell bathing solution serves as universal and extrasensitive messenger between external signal and the cell metabolic cascades. As Na:Ca exchanger is playing crucial role in regulation of intracellular Ca homeostasis, the minor modification of the intracellular calcium level dramatically changes the cell metabolic activity because the modulation of Ca-dependent enzyme systems.

Thus, on the basis of obtained data it was suggested that cell water medium serves as the second messenger between external factors and cell metabolism, while the cyclic nucleotides dependent Na:Ca exchanger is a gate for a metabolic cascade, through which the biological effect of EMF is realized. Obviously, to check this hypothesis and estimate the role of above mentioned pathways in realization of EMF biological effects on animals and human beings in different ecological condition, it is necessary more in detail different levels, starting from the distillate water up to the behavioral activity mammals, including human beings.

In this study it is very important to have adequate and unique equipment for dosemetry and estimation of EMF-induced effects. As EMF effect is very flexible, depending on different factors of external medium, for estimating of EMF hazardous dozes for different countries and regions it is necessary to consider the local ecological characteristic of medium and their modulation effect on EMF-induced biological effect. However, it isn't realistic to carry out such project for separate countries in region, because of the lack of expert magnetobiologists. Therefore, for facilitating the process of working out the principles of EMF standards harmonization under the conditions of different research educational and material potentials. So, it is evident that the cooperation of life scientists with physicists, chemists, biologists, physicians, cyberneticists, engineers and computer scientists is quite necessary. As the objective of Environmental Health Department of LSIEC is to promote co-operation, research, advanced training and exchange of information in environmental sciences in region, we try to call individual scientists, institutions and organizations to joint us in this field.

The program consists of the following sections:

1. The investigation of EMF effect on:
 - physicochemical parameters of water and water solution,
 - on functional activity of microorganisms,
 - biotechnological properties of foodstuffs,
 - the functions of isolated cells, tissues and organs,
 - the functions of a central nervous system and animal behavior,
 - visual system.
2. Epidemiological investigation of correlation between the intensity of electromagnetic radiation of a biomedium of regions and the level of some diseases (cancer, leukemia, sterility, etc.).
3. To make the maps of an atmospheric air pollution and intensity of electromagnetic radiation in regions.
4. On the basis of recommendations of WHO and obtained experimental data to develop the standards of allowable EMF doses for regions.
5. The development of unique equipment for EMF dosimetry and estimation of EMF-induced biological effect.



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Memorandum of UNESCO Seminar on
“Cellular Mechanism of Beneficial and Harmful Effects of Electromagnetic Fields”
September 24 – October 3, 2000
Yerevan, Armenia

Organized by:

Life Sciences International Educational School of Ministry of Education and Science of RA

Sponsored by:

World Health Organization

European Office of Aerospace Research and Development, Department of the Air Force

Office of Naval Research International Field Office, Department of the Navy

It is well known that, due to the progressive increasing of the number of EMF sources and dramatical changes of EMF spectrum, the electromagnetic field is the most dominant component of the spectrum of human environmental factors. The problem of EMF biological effect is becoming more and more important from the point of view of human health. Though at present the biological effect of EMF can be considered as a proven fact, the nature of the cellular target for EMF and the cellular mechanisms, through which its effect is realized, is not clear yet. Moreover, obtained experimental data on the cellular and molecular mechanisms of EMF in different laboratories are contradictive and difficult for interpretation. Numerous hypotheses on cellular mechanisms have been proposed, but none of them provided a reliable and exhaustive explanation of the experimental results. It is suggested that the main difficulty to accumulate the experimental data is due to the fact that different laboratories are using different methods to record the EMF-induced biological effect, which can be significantly modulated by other factors such as background radiation, acoustic waves, toxins temperature and etc. Therefore, to work out adequate methods for estimating the EMF induced biological effect, and to suggest unique criteria of its hazardous effect, there is need of multidisciplinary study of the cellular target for EMF and the metabolic cascades, through which the biological effect is realized. Obviously, it is impossible to solve such important and very complicated problems by the national potential of any separate regional country, the major part of which is living in hard economical situation and hasn't necessary research experience. We believe that international integration of research, educational and material potential of different countries in the framework of UNESCO and World Health Organization is very significant. One of the objectives of UNESCO CHAIR- Life Sciences International Higher Educational School (LSIHES) in Yerevan is to promote co-operation, research, advanced training, and exchange of information in environmental sciences. During last two decades the problem of the biological effects of the mechanical waves and ionizing and non ionizing radiation was one of the main subjects of investigations of the Biophysics Center and numerous research laboratories of Armenia. Taking into account the higher research potential and modern facilities of mentioned institutions, the

Environmental Health Department of LSIHES was organized. So, LSIHES can serve as regional research, educational and environmental health control Center, through which the international collaboration in this field can be realized. Therefore, we suggest individual researchers, institutions, foundations and organizations, the activity of which is focused on ecological and environmental health problems, to join us to gain all our aims. Here are the following projects, which need scientific and financial support.

1. "Molecular and Cellular Effect of Electromagnetic Field". Project is attached.
2. Fellowship grants for regional countries citizens' MS and Ph.D. study in LSIHES.
3. Special electronic equipment production destined for bioelectromagnetic purpose: dosimetry and estimated EMF effect.
4. Organization of regional environmental health laboratory.

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